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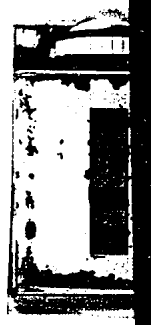

BASIC RESULTS OF USSR SCIENTIFIC RESEARCH ON RICKETTSIOSES IN 1954

Zhurnal Mikrobiologii, Epidemiologii, i Immunobiologii, No 6
Moscow, Jun 55

The following minutes and resolution were accepted by the expanded conference of the Subject Matter (Problem) Commission on Rickettsioses held 14-16 January 1955. Participants in the conference included: P. F. Zdrodovskiy (Moscow), Corresponding Member of the Academy of Medical Sciences USSR, chairman of the commission; M. M. Mayevskiy, Corresponding Member of the Academy of Medical Sciences USSR, member of the commission; S. M. Kulagin (Moscow), Candidate of Medical Sciences, member of the commission; L. V. Vasil'yeva (Moscow), Candidate of Medical Sciences; I. N. Kokorin (Moscow), Candidate of Medical Sciences, secretary of the commission; Prof K. N. Tokarevich (Leningrad); Prof A. V. Pshenichnov (Molotov); G. S. Mosing (L'vov), Candidate of Medical Sciences; Ye. G. Babalova (Tbilisi), Candidate of Medical Sciences; K. L. Gogoberidze (Tbilisi), physician; A. N. Sterkhova (Baku), Candidate of Medical Sciences; K. O. Leonidova (Odessa), Candidate of Medical Sciences; M. A. Mastenitsa (Tomsk), Candidate of Medical Sciences; M. Ya. Korn (Poti), Candidate of Medical Sciences; L. A. Manevich (Moscow), representative of the Main Sanitary Antiepidemic Administration, Ministry of Health USSR.

Q-Fever

In 1954, Q-fever was the principal subject of research at the Division of Rickettsioses (head, P. F. Zdrodovskiy), Institute of Epidemiology and Immunobiology imeni Gamaleya, Academy of Medical Sciences USSR. This research was carried out by a group of workers consisting of L. V. Vasil'yeva, S. M. Kulagin, Ye. M. Golinevich, N. K. Kekcheyeva, V. A. Yablonskaya, R. I. Kudelina, T. A. Bektemirova (an aspirant), I. N. Kokorin, N. N. Rybkina, and I. V. Tarasevich, The most important results of this work were as follows:

1. A method of culturing Burnet's rickettsiae on a large scale on chicken embryos has been developed, which assures the possibility of producing diagnostic antigens and vaccines from these rickettsiae.

2. The data on the high resistance of Burnet's rickettsiae to the action of physical and chemical factors, particularly to the effects produced by disinfectants, have been confirmed and supplemented.

3. The experimental forms of the Q-fever rickettsiosis in guinea pigs and white mice have been investigated in detail and the techniques to be applied in this type of work developed, thus assuring the availability of laboratory methods for all types of investigations on this rickettsiosis; furthermore, the histopathology of the Q-fever rickettsioses in laboratory animals has been investigated from the point of view of the techniques involved.

4. Using extensive material obtained in the course of 4,500 investigations, the serological methods of the diagnosis of Q-rickettsioses in human beings and animals have been developed as far as application of the reactions of complement fixation and agglutination are concerned. The allergic (intracutaneous) diagnosis of this rickettsiosis has been developed in a preliminary form, this method of diagnosis representing the simplest way of recognising an actual or former infection in human beings and animals.

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5. The technology of the mass production of diagnostic antigens from Burnet's rickettsiae has been developed and an instruction has been compiled which has been checked and approved by the State Control Institute.

6. In experiments on guinea pigs a method of preventive inoculation against the Q-rickettsiosis has been successfully developed. This procedure assures good immunological results on the basis of its preliminary investigation on human beings (about 50 persons).

7. The technology of the mass production of a prophylactic vaccine against human Q-fever has been developed and an instruction has been compiled on its production, control, and application. This instruction has been confirmed by the Serum-Vaccine Commission and the use of the vaccine on 5,000 persons exposed to the danger of infection has been permitted.

8. In experiments on mice the chemotherapy of the Q-rickettsiosis has been investigated. In the course of this work the high effectiveness of biomycin, aureomycin, terramycin, and riomycin and the low effectiveness of levomycetin have been established.

9. In a mass serological investigation of clinical patients and convalescents suspected of having had Q-fever, of workers at meat combines and dairy plants, and of blood donors in 37 populated localities of seven oblasts of the central and southern territories of the European part of the USSR and of five oblasts of Central Asia, it was found that 14.5 % of all those investigated (3,181 persons) exhibited a positive reaction of complement fixation. Cultures of Burnet's rickettsiae were isolated from the sick persons examined.

10. It has also been established that various farm animals (cows, sheep, goats, horses, and dogs) are infected with rickettsiosis. In the 1,348 cases investigated, 13.7 % of positive results were obtained when the reaction of complement fixation was carried out with the serum. Cultures of rickettsioses were isolated from cows' milk and from the dust of the barns where the cows had been kept.

11. Work carried out together with the Division of Parasitology (head, P. A. Petrishcheva) at natural reservoirs of the Q-rickettsiosis established that pasture and Argasidae ticks and Gamasidae mites are infected with the causative factor. As far as Gamasidae mites are concerned, this finding was made for the first time. Theoretical investigations also established that some wild animals, for instance "dzheyrans" [Gazella subgutturosa] and gerbils, are infected with Q-fever.

12. It has been established that human beings are infected principally from cows, sheep, and goats (when the causative factor is present in the milk) and possibly also from other animals (horses and dogs.) Animals presumably get the infection predominately from ticks.

13. Among the ways in which infection takes place, one must mention transmission through the air and dust, alimentary infection as a result of the consumption of milk, and contact infection at meat combines. In two cases there was the possibility that the infection was transmitted through water. Cases of imported infection have been studied, such as the outbreak of Q-fever at the Carpet-Plush Combine, which used wool brought from Turkmenia.

14. Q-fever, which is a new type of rickettsiosis of the USSR, has been subjected to many comprehensive investigations in 1954.

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In addition, the following information on Q-fever has been communicated:

E. N. Sterkhova reported on the results of a serological investigation of cattle and other farm animals in Azerbaydzhan, which has established with certainty the occurrence of Q-rickettsiosis among the animals. Among 289 cows that have been investigated, the positive reaction of complement fixation was detected in 10 %. A high incidence of this infection also occurs among sheep.

In accordance with what has been said above, among 820 persons who were released from Baku hospitals after being treated for various diseases, 8.3 % showed a positive serological reaction for Q-fever (retrospective diagnosis). In connection with this work, the isolation of the causative factor and the infection with it of guinea pigs is expected.

Prof K. N. Tokarevich reported on two cases of Q-fever which have been diagnosed serologically at Leningrad. Among the patients examined there were imported cases and cases of infection connected with work on imported raw material (skins, etc.)

On the basis of the data which have been reported and also of data published earlier by workers at Central Asiatic institutes and at the Institute of Virology, Academy of Medical Sciences USSR (Prof M. P. Chumakov et al), the conference unanimously agreed that Q-fever represents a genuine problem in the USSR and should be subjected to further investigation.

The conference considered the most important problems in connection with the investigation of Q-fever, particularly at the periphery, to be the following:

1. Investigation of the geographic distribution of the Q-rickettsiosis in the country, serological examination of workers at meat combines and dairy plants, testing of the blood at blood donor stations, and testing of samples of serum which are sent to laboratories for various investigations

2. Study of the relative importance of the Q-rickettsiosis in the pathology of human infections and investigation from this standpoint of patients at clinics of infectious diseases and at hospitals

3. Many-sided investigation of the epidemiology of Q-fever and parallel investigations carried out on farm and domestic animals by the veterinary laboratories network

4. An extensive investigation of the clinical aspects of Q-fever and of its therapy by means of antibiotics (biomycin)

5. Development of measures against the Q-rickettsiosis combined with the sanitation of sources from which it spreads (work done in conjunction with veterinary organizations)

In accordance with the statements made above, the conference charged the chairman of the Subject Matter Commission with the execution of the following measures:

1. Representations to the Scientific Council of the Ministry of Health USSR in regard to a most speedy assignment of personnel and funds for work at the newly organized rickettsiosis laboratories

2. Making a request to the Scientific Council that problems in connection with Q-fever be given the highest priority in the plans of work to be carried out at rickettsiosis laboratories

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3. Requesting the Scientific Council to inform the ministries of the union republics in regard to the importance of investigations pertaining to the problem of the Q-rickettsiosis

4. Urging the Scientific Council to organize an interinstitutional commission on the Q-rickettsiosis in which the ministries that are interested in the subject will be represented

The conference lauded the decision of the Division of Rickettsioses, Institute of Epidemiology and Microbiology imeni Gamaleya, Academy of Medical Sciences USSR, to donate Q-antigen for use in investigative work to be done by the rickettsiosis laboratories of Leningrad, Tomsk, L'vov, Odessa, Tbilisi, and Baku.

At the same time, the conference asked the Scientific Council to render aid to the organization without delay of the mass production of Q-antigen.

Epidemic Typhus

The problems connected with epidemic typhus, particularly its residual form, were investigated primarily at the Molotov Virological Laboratory, the Rickettsiosis Laboratory of the Leningrad Institute imeni Pasteur, and the Rickettsiosis Laboratory of the L'vov Institute of Epidemiology and Microbiology. The principal results of this work can be summarized as follows:

1. According to a communication by A. V. Pshenichnov, a variety of clothes lice has been developed, at the Molotov laboratory directed by him, which can feed on the blood of rabbits. This variety was developed by a prolonged process of adaptation extending over three years.

2. According to Pshenichnov, a specific variety of Prowazek's rickettsiae has been obtained as a result of uninterrupted passages through lice extending over 12 1/2 years, which does not produce an experimental infection in guinea pigs and exhibits a low toxicity towards mice. This strain is of interest as a possible source of a live vaccine. Investigation of the strain is being continued.

3. In the course of the investigation of residual forms of typhus, A. V. Pshenichnov and G. S. Mosing in analogous studies of the typhus infection in guinea pigs, in connection with which the control was carried out by infecting lice with suspensions from various organs of the experimental animals, made the following findings: on the basis of data obtained by both investigators, which are in complete agreement, the maximum concentration and the longest preservation of the virus was found to occur in the kidneys and in the spleen (according to Pshenichnov, also in the lungs).

According to A. V. Pshenichnov, the latent forms of the typhus infection do not occur in guinea pigs, while according to G. S. Mosing's data, the rickettsiae can be detected in the spleen and in the kidneys of these animals for a period of 21 days after cessation of the fever. Furthermore, according to Mosing, the rickettsiae can be isolated in 4 % of the cases 86 days after infection.

4. Mosing points out that he has discovered sporadic forms of typhus in rural regions. In some patients suffering from recurrent typhus the rickettsiae could be isolated by using lice up to the 10th day and 15% of these cases could be identified as Prowazek's rickettsiae. Mosing has developed a method of macroscopic drop agglutination of Prowazek's rickettsiae with an antigen prepared from

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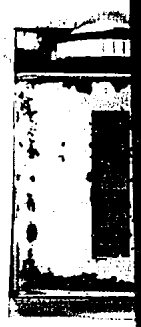

infected lice. This reaction has been introduced into practical use in the Ukraine and yields good results. Mosing emphasizes this reaction's unsuitability for microagglutination.

5. According to a communication by K. N. Tokarevich, he has observed cases of recurrent typhus which occurred at hospitals. Strains of rickettsiae could be isolated from patients by feeding lice on them. These strains were isolated after repeated passages in 15% of the cases. Fifteen strains were investigated which proved to be identical with Prowazek's rickettsiae.

6. Experimental data from the Division of Rickettsioses, Institute imeni Gamaleya (I. V. Tarasevich), and epidemiological investigations by K. N. Tokarevich at Leningrad did not confirm the assumption that typhus may be transmitted by Gamasidae mites.

7. In their interpretation of recurrent typhus, G. S. Mosing and K. N. Tokarevich confirm the relapse theory, which is disputed by Pshenichnov.

The conference pointed out the desirability of continuing the discussion on this subject in the journals and the necessity of instituting an extended discussion of this matter at the forthcoming conference on rickettsioses. At the same time the conference recommended the continuation of work aiming at the clarification of the nature of sporadic typhus in accordance with the program accepted earlier.

Murine Typhus

Ye. G. Babalova (Tbilisi) presented detailed data on murine typhus in Georgia. In addition to rats, rickettsiae have been detected in mice. The human infection with this disease and infection of rodents occur not only in the ports of the Black Sea, but also in the interior of the country along railroads.

In two cases the occurrence of murine typhus was established in the mountains at a distance of 40 kilometers from the railroad. Murine typhus can be easily differentiated serologically from epidemic typhus when antigens of appropriate quality are used. According to Babalova, the antigen supplied by the Institute imeni Gamaleya is not suitable. This investigator expressed the assumption, which is supported by epidemiological and clinical data, that in a number of cases a diagnosis of typhus is made on the basis of a recrudescence of an anamnestic reaction for rickettsiae under the influence of other diseases. In other words, the serological diagnosis occasionally leads to incorrect conclusions.

Taking into consideration the proven existence of foci of murine typhus, the conference recommended that the rickettsiosis laboratories in Tbilisi (Ye. G. Babalova) and in Baku (A. N. Sterkhova), which enter into the composition [organization] of the local institutes of epidemiology and microbiology, continue work on this rickettsiosis. The same recommendation was made as far as the Rickettsiosis Laboratory at Odessa, directed by K. O. Leonidova, is concerned. The conference also recommended to the Baku Institute of Epidemiology and Microbiology (A. N. Sterkhova) that it give the necessary guidance, as far as methods of serological diagnosis of murine typhus are concerned, to the Hospital imeni Semashko at Baku.

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Volyn' Fever [Trench Fever]

A. V. Pshenichnov made a communication to the effect that at the Molotov Laboratory, directed by him, an artificial medium has been developed in recent years on which the causative factor of Volyn' fever can be cultured. The culture of the rickettsiae of Volyn' fever is used in laboratory work as an antigen for the reaction of complement fixation. The conference took note of the information in question.

Rickettsial Antigens and the Organization of Their Production

The conference considered the state of serological diagnosis and particularly of the serological diagnosis of diseases of the typhus and Q-fever groups completely unsatisfactory.

The reasons for the existence of the situation referred to are, on the one hand, shortages in the supply of antigens combined with a virtually complete lack of Q-antigen, and on the other hand, deficiencies in standardization which result in variations in the quality of the antigens that are being supplied. Furthermore, the available antigens are much too expensive, the price being 6,000-12,000 rubles per liter.

Differences in the quality of the methods of serological diagnoses that are being recommended have a disorienting effect on the laboratories.

The conference emphasized that the antigens derived from Prowazek's rickettsiae and Rickettsiae mooseri, which are supplied by the production sector of the Institute of Epidemiology and Microbiology imeni Gamaleya, meet with the greatest amount of criticism. These antigens are badly standardized and often are unsuitable both for direct and differential serological diagnosis.

Completely unsuited for use is the method of microagglutination recommended by the Typhus Division of the Institute imeni Gamaleya.

Taking into consideration the particular significance which methods of serological diagnosis have in the case of rickettsial diseases, especially of typhus and Q-fever, the conference informed the Scientific Counsel of the necessity of carrying out the following measures:

1. One must make certain that rickettsiosis antigens of high quality and in sufficient quantity be produced and should specifically organize without delay the production of Q-antigen from Burnet's rickettsiae. In the opinion of the conference, the aid of the following institutes must be sought in this task:

The Typhus Division (head, M. K. Krontovskaya), Institute imeni Gamaleya at Moscow; the rickettsiosis laboratory being organized at the Institute of Vaccines and Sera at Leningrad; the Virological Laboratory at Molotov (head, A. V. Pshenichnov); the Rickettsiosis Laboratory of the Institute of Epidemiology and Microbiology at L'vov (head, G. S. Mosing); and in the future also the rickettsiosis laboratory being organized by the Institute of Vaccines and Sera at Tomsk. To both the L'vov and Molotov laboratories, which produce antigens from infected lice, should be recommended right now the organization of the production of rickettsiosis antigens from egg cultures according to an instruction tested and approved by the Control Institute after its confirmation by the Serum-Vaccine Commission.

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The divisions and institute laboratories which are to be engaged in the production of rickettsiosis antigens should be reinforced by supplying the necessary technical means and personnel on the basis of their requisitions.

2. To expedite the standardization of serological diagnosis, one should charge the Subject Matter Commission on Rickettsioses with this task, imposing on the commission the duty to review immediately the instructions in force so that conclusions can be drawn in respect to the methods involved. All drafts of instructions dealing with this matter should be subjected to a preliminary review by the Subject Matter Commission.

3. To assure the availability of the necessary quantity of rickettsiosis antigens, one must impose on the Control Institute the duty of checking the diagnostic effectiveness of the antigens being released. This activity must be carried out by agreement with the Subject Matter Commission. In connection with this, it should be recommended to the production sector of the Institute imeni Gamaleya that they take steps to assure that the rickettsiosis antigens being supplied [by it] are of good quality. Particular attention should be paid to their purification from tissue admixtures.

4. The Scientific Council should be requested to initiate at the Main Sanitary-Antiepidemic Administration of the Ministry of Health USSR steps aimed at the revision and reduction, as far as this is possible, of the prices for rickettsial antigens.

Status of Available Rickettsiosis Laboratories
and Projected Network of Virus-Rickettsiosis Laboratories

The conference regarded with satisfaction the project of the organization of a network of virus-rickettsiosis laboratories, but at the same time expressed astonishment and regret with regard to the circumstance that the problem of available rickettsiosis laboratories in the periphery has not received any attention and that the status of these laboratories has worsened rather than improved. Thus, the Rickettsiosis Laboratory of the Leningrad Institute imeni Pasteur (head, Prof K. N. Tokarevich) and the Rickettsiosis Laboratory of the L'vov Institute of Epidemiology and Microbiology (head, T. S. Mosing) do not receive any assistance which would advance work on the subject matter assigned to them, although these laboratories are in urgent need of additional funds and equipment.

For instance, the Virological Laboratory at Molotov (head, Professor A. V. Pshenichnov), which has worked successfully in the field of rickettsioses for many years, is to be closed according to a decision of the Molotov Oblast Executive Committee of 3 December 1954.

The conference also noted the lack of coordination evident in the organization of new laboratories in localities where rickettsiosis laboratories already exist. This situation has developed at Leningrad with reference to the Institute imeni Pasteur and the Institute of Vaccines and Serums.

Accordingly, the conference recommended:

1. That the Molotov Virological Laboratory be under all conditions preserved and that, on the basis of this laboratory, the rickettsiosis laboratory projected for the Molotov Institute of Vaccines and Serums be built up; and that, furthermore, rickettsial antigens be produced at this laboratory

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2. That the Rickettsiosis Laboratory of the Leningrad Institute imeni Pasteur be reinforced by assigning to it additional personnel (two laboratory technicians and two persons engaged in preparations) and that the necessary equipment be supplied to it, as required; and that, furthermore, the rickettsiosis laboratory projected for the Leningrad Institute of Vaccines and Serums be subordinated to this laboratory, as far as methods are concerned, and that provision be made for the production of rickettsiosis antigens and vaccines at the laboratory of the Institute of Vaccines and Serums

3. That the Rickettsiosis Laboratory of the L'vov Institute of Epidemiology and Microbiology be reinforced by adding two laboratory technicians and two persons engaged in preparations, and supplied with additional equipment as required, and that, furthermore, provisions be made for the mass production at this laboratory of rickettsiosis antigens to be used in the Ukrainian SSR

4. That the Division of Rickettsioses of the Institute of Epidemiology and Microbiology imeni Gamaleya be reinforced as a microbiological center and center for the training of personnel to be engaged in work on rickettsioses, and that, furthermore, the necessary equipment for this purpose, as required by the institute, and funds be provided within the limits fixed by the Presidium of the Academy of Medical Sciences USSR on 3 March 1954

5. That personnel and equipment as planned and funds be furnished to the virus-rickettsiosis laboratories of the Tomsk, Leningrad, Molotov, and Odessa Institutes of Vaccine and Serums where the conference has planned work on rickettsioses having the highest priority, particularly with regard to Q-fever, and including the production of rickettsiosis antigens at Leningrad, Molotov, and Tomsk

6. That the laboratories of oblast and city sanitary-epidemiological stations which are engaged in work similar to that done at the virus-rickettsiosis laboratories of the institutes be systematically subordinated to the institute laboratories and organizationally merged with them.

Organization of a Conference on Rickettsioses

The conference regarded with satisfaction the decision of the Presidium of the Academy of Medical Sciences USSR of 3 March 1954, which points out the necessity of calling a conference on rickettsioses. The timeliness and absolute necessity of such a conference are confirmed.

The conference entrusted the Subject Matter Commission with drawing up the program of the conference on rickettsioses and with making the necessary representations to the Academy of Medical Sciences USSR in that connection.

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